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MORPHOLOGICAL FORMATION OF BONE TISSURE IN HYPOPARATHYROIDISM

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Abstract:
This study is devoted to studying the effect of changes in the functional activity of the parathyroid glands on the morphological intensity of tubular bone formation. Experimental modeling of hypoparathyroidism in laboratory rats (n = 30) was carried out and the dynamics of morphological changes in the process of tubular bone ossification was analyzed. Based on the results of morphological research methods, the dynamics of the formation of tubular bones is revealed, and the patterns of ossification of bone tissue against the background of hypoparathyroidism are also established. As a result of the study, a difference was shown from the normal histological picture of hypoparathyroid individuals in the growth zones, namely the basal layer, the chondrocytes are vacuolated. The appearance of young osteoblasts is determined in some places; they are arranged as multidirectional architectonics.

Keywords: Parathyroid Gland; Chondrocyte; Hypoparathyroidism; Hypocalcemia; Hyperphosphatemia; Tubular Bones.

INTRODUCTION

Hypoparathyroidism in most cases is characterized by a decrease in the function of the parathyroid glands and a decrease in the production of parathyroid hormone, but peripheral forms resulting from the resistance of cells and tissues of the body under the action of parathyroid hormone are also known. Hypoparathyroidism of various origins is observed in 0.2–0.3% of the population [H. Singh, 2005]. Most often, adult hypoparathyroidism develops after surgical removal or damage to the parathyroid glands, which most often occurs after thyroidectomy for thyroid cancer or Graves' disease, repeated or extensive operations for other diseases of the thyroid gland, neck and upper mediastinum, as well as after surgical interventions in the treatment of primary or secondary hyperparathyroidism. After operations on the thyroid gland due to Graves disease, the incidence of transient hypocalcemia is about 3.1% [Roca-Cusachs A., 1997; Simonetti G., 2007], and persistent hypoparathyroidism occurs in 1% of cases [Basil M. 2001]. Among other known causes of hypoparathyroidism are:

a) abnormal development of the parathyroid glands (congenital agenesis or hypoplasia of the glands);
b) destruction of the parathyroid glands in autoimmune diseases;
c) a decrease in the function of the parathyroid glands due to impaired secretion or production of parathyroid hormone;
d) syndromes of resistance to parathyroid hormone (hypomagnesemia, pseudohypoparathyroidism).

All described forms have a similar pathogenesis and clinical picture, differing only in etiological aspects.

A lack of parathyroid hormone in turn leads to an increase in the level of phosphorus in the blood due to a decrease in the phosphaturic effect of the parathyroid hormone on the kidneys, as well as hypocalcemia due to a decrease in calcium absorption in the intestine, a decrease in its mobilization from the bones, and insufficient calcium reabsorption in the renal tubules. In the genesis of hypocalcemia, a decrease in the synthesis of the active metabolite of vitamin D, calcitriol, whose production depends on the parathyroid hormone, is important. The main clinical manifestations of hypoparathyroidism are caused by hypocalcemia and hyperphosphatemia, which leads to an increase in neuromuscular excitability and general autonomic reactivity [1,3].

All of the above dictates the need for further study of the intensity of osteogenesis in the morphological aspect of hypoparathyroidism and determines the relevance of the study.

Purpose of the study. To study the effect of parathyroid hormone deficiency on the morphological intensity of the process of ossification of the tubular bones.

The objectives of the study.

1. To determine the optimal experimental model

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of hypoparathyroidism in rats.

2. To reveal the dynamics of the morphological features of the long tubular bones of rats at different ages of the control group.
3. To study the morphological changes in the formation of tubular bones with hypoparathyroidism.
4. Determine microanatomical changes in the structure of the tubular bones in hypoparaterioid rats

MATERIALS AND METHODS

Experimental modeling of hypoparathyroidism in laboratory rats (n = 30) was carried out and the dynamics of morphological changes in the process of ossification of tubular bones was analyzed.

The material was the tubular bones of rats with hypofunction of the parathyroid gland.

The experiments were performed on 30 white rats weighing 135 ± 1.2 g. Given the significant impact on the condition of animals of the exchange of minerals, weight, their age and composition of the diet, when conducting experiments, we observed identical conditions.

Experimental studies were carried out in two series: series I - animals of the control group, series II - animals with hypoparathyroidism. For each series, 15 rats were used. The characteristics of the starting animals of individual series of experiments are shown in table.

In the first control series in animals, themorphological structure of the bone tissue of the tubular bones was investigated. In the second series, hypoparathyroidism was induced in animals with electrocoagulation of the upper grains of the parathyroid gland by surgery.

All rats were kept under identical vivarium conditions. The conditions of the experiment and the decapitation of animals were in accordance with theprovisions of Order No. 742 of November 13, 84, "On the Use of Experimental Animals", as well as the international rules "Guide for the Care and Use of Laboratory Animals".

Research Methods. The hypoparathyroi-dism model was induced by the removal of the upper grains of the parathyroid gland. For histological examination, tissue pieces from various elements of rat tubular bones were fixed in Carnoy fluid and in a 12% solution of neutral formalin, dehydrated in alcohols of increasing concentration and embedded in paraffin. Sections 5-8 microns thick were stained with hematoxylin eosin and according to the Van Gieson method.

For histological examination, tissue pieces from various elements of rat tubular bones were fixed in Carnoy fluid and in a 12% solution of neutral formalin, dehydrated in alcohols of increasing concentration and embedded in paraffin. Sections 5-8 microns thick were stained with hematoxylin eosin and according to the Van Gieson method. Neutral mucopolysaccharides were detected by the SHIK reaction, and acidic ones were detected with toluidine blue. Morphological studies were performed on experimental material taken from the elements of tubular bones in control rats and in experimental hypoparathyroidism [5,7,8].

The study and creation of experimental models of skeletal deformities contribute to the search and implementation of effective methods for early detection and treatment of this pathology. Meanwhile, thisrequires accurate knowledge of the normal structure of bone formation structures in the morphological aspect. We conducted our research on rat pups.

During histological examination in all control animals in the epiphyses of the tubular bones, the places of attachment of the articular bag are determined, where the fibrous capsule and elements of the synovial membrane are well identified.

The synovial layer of the capsule is characterized by uneven thickness, which is due to the growth of granulation tissue of various maturity, rich in blood vessels. The walls of blood vessels of uniform thickness are clearly defined. Endotheliocytes of various maturity lie in it.

In some preparations, the synovial membrane is constructed of fibrous connective tissue structures, sometimes with very short villi. Collagen fibers without signs of swelling fit tightly together.

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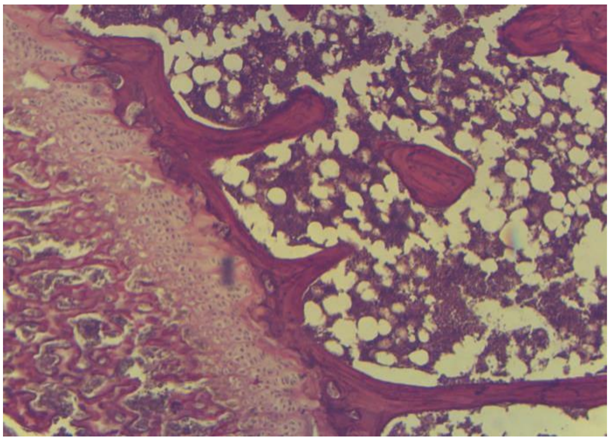

Fig. 1 Bone plate (A) and bone marrow (B). Stained by Van Gieson. Magnification 10 × 40

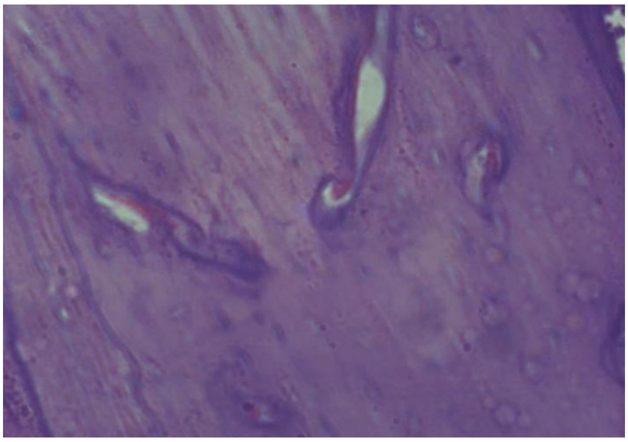

Fig. 2 Periosteum of the femoral head. Hematoxylin-eosin stain. Magnification 10 × 40

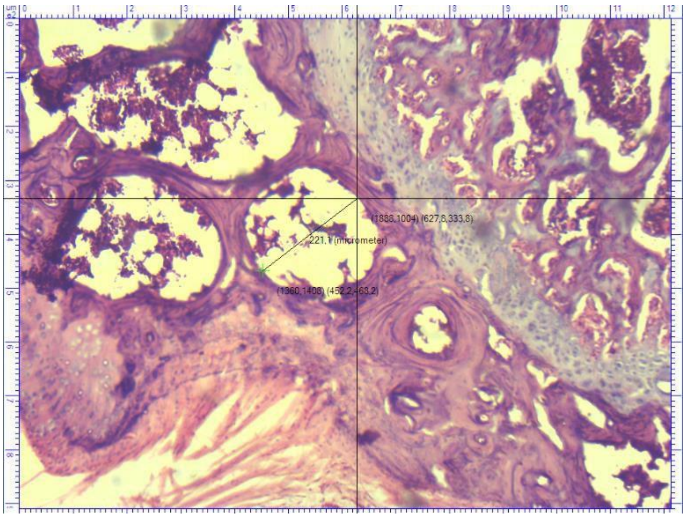

Fig. 3 The cartilaginous part of the femoral head with well-stained basophilic chondrocytes (A) and a densefibrous connective tissue capsule (B). Hematoxylin-eosin stain. 7 × 10 magnification

Part of the pineal gland (head) of the femur is formed from cartilage, which consists of chondrocytes located on the surface perpendicular to the columns. In the depths they lie with longitudinal nests, and young cartilage cells with basophilic nuclei are visible on the periphery. The head is surrounded by a dense connective tissue capsule.

In the metaphysis area, there is a zone with well-stained cellular elements. Osteoblasts and newly formed bone beams are located along the edge. A dense capsule (fibrous bag) and synovial membrane are formed around a fragment of the future bone (Fig. 3.4). The intercellular substance is homogeneous, more intensively colored towards the center.

In the next zone, the formation of bone beams that grow to the periphery is traced. Perichondral and enchondral ossification is observed. Therefore, the whole picture corresponds to normal osteogenesis, i.e. bone formation instead of cartilage. Osteoblasts and osteocytes are clearly defined in the beams.

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The results of histochemical studies showed that in hyaline cartilage of the femoral head and articular cavity in significant quantities there are both acidic and neutral mucopolysaccharides.

Glycogen is found in the deep zones of cartilage, which, apparently, is associated with the intensity of metabolic processes in these zones and is the initial product in the synthesis of chondrotin sulfate.

The predominant localization of acid mucopolysaccharides is also observed in deep zones, which is explained by the diffusion of nutrients, mainly through these zones. The synthesis of chondrocytes with mucopolysaccharides in the articular cartilage is indicated by the presence of an abundant amount of components in the immediate vicinity of the cell.

Thus, the main physicochemical properties of cartilage are associated with the state of protein-polysaccharide matrix complexes. The localization of the detected groups mainly corresponds to the distribution of mucopolysaccharides in the cartilage and bone tissue of the femoral head and articular cavity. Probably, all processes in the articular cartilage are carried out by protein-polysaccharide complexes.

Scientific novelty. Based on the results of morphological research methods, the dynamics of the formation of tubular bones is revealed, and the patterns of ossification of tubular bones for the first time against hypoparathyroidism are also established.

As a result of a detailed analysis of morphological changes, practical recommendations have been prepared for the development of preventive and therapeutic measures for limb deformation against the background of decreased parathyroid function.

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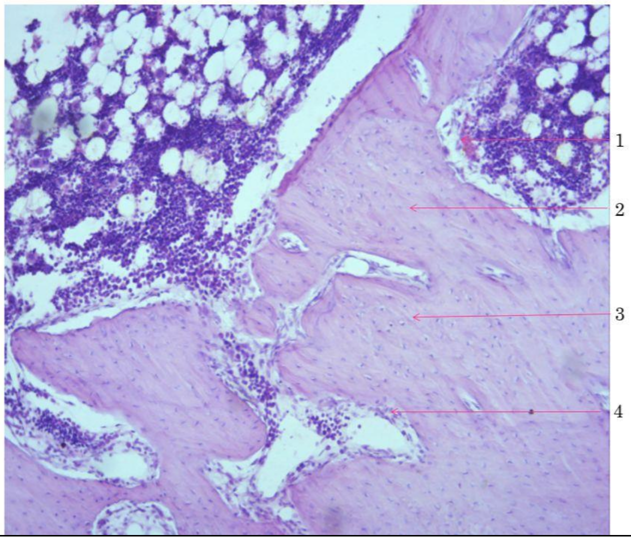


Fig. 4 Compact part of diaphysis. Magnification 10 × 40

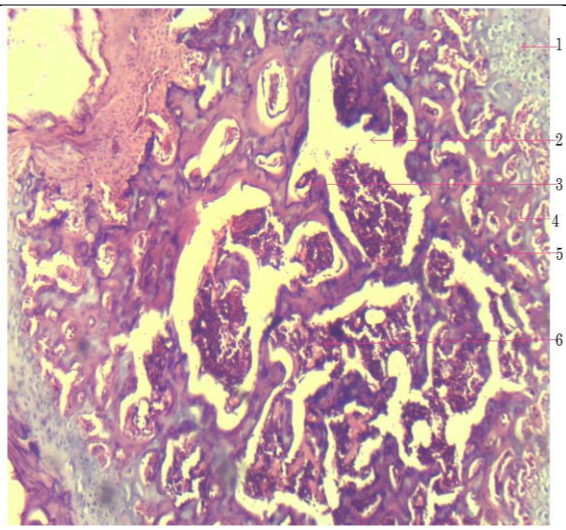
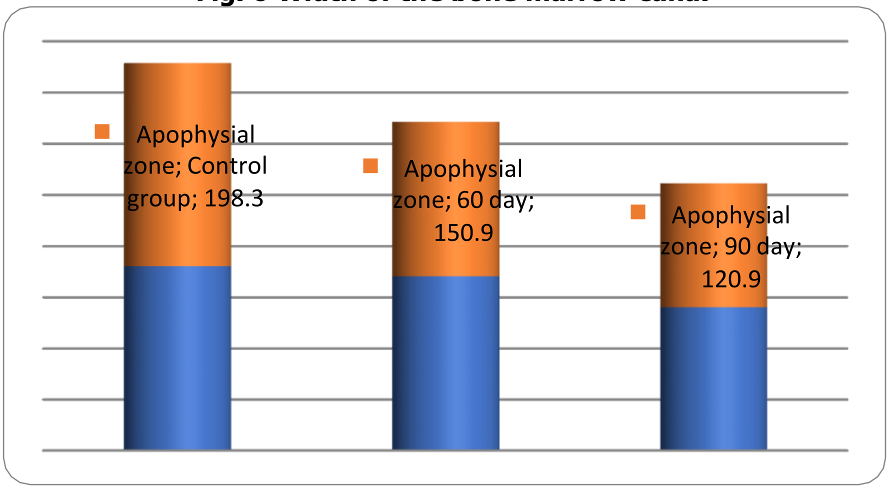


Fig. 5 Epifysar enchondral ossification. Magnification 10 × 4

Fig. 6 Width of the bone marrow canal



Practical significance. The results of the study will serve as the basis for the modification of the available classification and diagnostic criteria for hypoparathyroidism. The revealed signs of an unfavorable prognosis in the early stages of the disease justifies the need to take into account the debut option and the course of juvenile disease when choosing patient treatment tactics.

The main manifestation of hypoparathyroidism is hypocalcemia, which is due to the fact that a deficiency of parathyroid hormone leads to insufficient mobilization of calcium from the bones, a decrease in calcium reabsorption in the renal tubules, and also to a decrease in calcium absorption in the intestine.

The level of serum ionized calcium is directly dependent on the parathyroid hormone and 1.25 (0H)

The main place among the causes of hypoparathyroidism (up to 95%) is occupied by postoperative hypoparathyroidism, which is often due todamage or removal of the parathyroid glands during surgery, as well as hemorrhage in them or the development of fibrotic processes at the site of the operation in the long term.

The frequency of postoperative hypoparathyroidism associated with radical interventions on the thyroid

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gland, according to different authors, ranges from 0.5 to 50%. Many factors affect the incidence of postoperative hypoparathyroidism: surgeon's experience, volume of surgery, total thyroid volume, reoperation, and the inability to determine all four parathyroid glands during surgery.

Distinguish between transient and persistent (6 months or more after surgery) postoperative hypocalcemia. The prevalence of transient hypocalcemia, according to different authors, is 20-40%, persistent - 5-7%.

The development of hypocalcemia after operations on the parathyroid glands due to hyperparathyroidism is characteristic. In such cases, hypoparathyroidism is associated with removal of the most active tumor tissue, while the suppressed activity of the remaining parathyroid glands leads to a sharp drop in serum parathyroid hormone and calcium levels. The concomitant pathology of the skeletal system contributes to the development of the syndrome of "hungry bones", which leads to increased absorption of calcium and phosphate by the bones, which even the intact parathyroid gland cannot compensate for these changes.

A decrease or excess of magnesium can lead to hypocalcemia and, as a result, to functional hypoparathyroidism. Magnesium is necessary for the secretion of parathyroid hormone and the activation of parathyroid hormone receptors by a ligand. With hypomagnesemia, the level of parathyroid hormone is low or is on the lower boundary of the normal range, in the presence of slight hypocalcemia. Magnesium, like calcium, can activate extracellular calcium-sensitive receptors and inhibit the secretion of parathyroid hormone. Loss of magnesium is observed due to gastrointestinal upsets, as well as alcoholism. After correcting the level of magnesium, the ability to secrete parathyroid hormone by the parathyroid glands and their sensitivity to it are restored.

With all syndromes of resistance to parathyroid hormone, against the background of an increased level of parathyroid hormone, hypocalcemia and hyperphosphatemia are observed, associated with the resistance of target tissues to the action of parathyroid hormone. Therefore, they are referred to by the general term "pseudohypoparathyroidism". Normalization of calcium levels with pseudohypoparathyroidism usually leads to a decrease in the level of parathyroid hormone, but does not eliminate the resistance of target tissues to parathyroid hormone.

In chronic hypocalcemia due to hypoparathyroidism, exostoses and foci of calcification occur in soft tissues. Periarticular deposits of calcium salts are often accompanied by chondrocalcinosis and pseudogout.

Bone loss in the peripheral skeleton is first detected in the end sections of the tubular bones due to the predominance of the trabecular bone. Endostatic resorption plays a dominant role in HPT. The result is a broadening of the medullary canal with a thinning of the cortical layer. It was previously believed that the most characteristic manifestation of bone tissue damage was generalized fibrocystic osteitis, detected in 50% of cases. However, in recent years, in connection with an earlier diagnosis of the disease, fibrocystic osteitis is observed less and less (10-15%). Bone demineralization leads to skeletal deformity, pathological fractures, compression destruction of the spine, in connection with which there is a decrease in growth of 2-4 cm, the appearance of neurological symptoms, manifested by radicular syndrome, pelvic girdle paralysis, paresthesias, decreased tendon reflexes. On radiographs, characteristic changes are visible: erosion of the external cortical surface, generalized demineralization, local destructive processes, often cystic. A histological examination of bone lesions reveals a decrease in the number of trabeculae, an increase in multinucleated osteoclasts, and the replacement of cellular and bone marrow elements with fibrovascular tissue. One of the most common places for the formation of cystic changes is the lower, less often the upper jaw.

At present, three-energy X-ray absorptiometry is a method for assessing and studying bone mineral density, this method is simple to use and has a low radiation load, which allows it to be performed repeatedly and to evaluate the dynamics of the state. It is the measurement of bone mineral density that underlies the diagnosis of osteoporosis and is one of the most important and early indicators of bone pathology, especially in connection with an increased risk of fractures with a decrease in bone mineral density. In recent years, considerable experience has been gained with the use of three-energy X-ray absorptiometry in the study of osteoporosis and in predicting the risk of fractures in the general population. Currently, with GPT, diffuse bone damage is most often detected, which is difficult to distinguish due to the age and gender of patients from postmenopausal osteoporosis. The definition of osteoporosis was developed by WHO and is based on the determination of bone mineral density at any point according to the T-criterion. Indicators of the T-criterion from +2.5 to -1 standard deviations from

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peak bone mass are considered a normal indicator of bone mineral density. Osteopenia - indicators of the T- criterion -1 standard deviations and below. Severe osteoporosis - indicators of the T- criterion of -2.5 standard deviations and lower with a history of one or more fractures.

CONCLUSION

Results of the conducted researches allow to characterize in focal dystrophy of hondrotsit and in braking of osteogenesis on a surface of a rostkovy zone. In more remote period of experiment dedifferentiation of superficial and transitional layers of a gialinozny cartilage in fibrous fabric came to light.

In deep layers of a cartilage signs of decrease in proliferative processes and increase degenerate were noted that led to an osteogenesis perversion on growth zone surface.

Narrowing of a zone of enkhondralny growth due to disappearance of a layer the proliferation of hondrotcit, probably, preceded its fastest closing.

The revealed histologic changes in components of tubular bones can promote forecasting of results of treatment of deformations of a skeleton, and also their complications.

Part of the pineal gland (head) of the femur is formed from cartilage, which consists of chondrocytes located on the surface perpendicular to the columns. In the depths they lie with longitudinal nests, and young cartilage cells with basophilic nuclei are visible on the periphery. The head is surrounded by a dense connective tissue capsule.

In the metaphysis area, there is a zone with well-stained cellular elements. Osteoblasts and newly formed bone beams are located along the edge. A dense capsule(fibrous bag) and synovial membrane are formed around a fragment of the future bone. The intercellular substance is homogeneous, more intensively colored towards the center.

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The predominant localization of acid mucopolysaccharides is also observed in deep zones, which is explained by the diffusion of nutrients, mainly through these zones. The synthesis of chondrocytes with mucopolysaccharides in the articular cartilage is indicated by the presence of an abundant amount of components in the immediate vicinity of the cell.

Thus, the main physicochemical properties of cartilage are associated with the state of protein-polysaccharide matrix complexes. The localization of the detected groups mainly corresponds to the distribution of mucopolysaccharides in the cartilage and bone tissue of the femoral head and articular cavity. Probably, all processes in the articular cartilage are carried out by protein-polysaccharide complexes.

The results of histological studies showed that homogenization is observed in the collagen fibers of the fibrous capsule, and in some places the cellular elements are not detected at all. Among the fibrous structures, the formation of the joint space takes place. The joint gap is narrowed due to an increase in connective tissue.

In some preparations, proliferation of connective tissue, plethora and thrombosis of the vessels of the round ligament are noticeable. The femoral head consists of a homogenized newly formed cartilage with poorly stained chondrocytes. In most cartilage cells, hypochromia of the nuclei is noted, and in some places - pictures of necrobiosis and necrosis. The places of attachment of fibrous structures to the head of the femur of loose fibrous tissue are traced.

The degenerative degenerative changes in the cartilage of the greater trochanter are clearly defined. The cytoplasm of most chondrocytes is strongly vacuolated, necrobiosis and necrosis of chondrocytes are well defined. In the metaphysis zone, thin bone beams and cavities filled with fatty bone marrow are detected. Bone beams are coarse-fibered, located on the periphery, and the cavity of the medullary canal is defined inside. Therefore, the nature of the revealed changes indicates a delay in osteogenesis in the state of rat hypoparathyroidism, which significantly affects the development of bone formation.

Histological studies revealed the detection in the cartilaginous coated femoral heads with moderately severe vacuole dystrophy. Along with well-stained chondrocytes, most cartilage cells show hypochromia of the nuclei, and in some places - a picture of necrobiosis and necrosis.

Cartilage cells with vacuole dystrophy, foci of

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necrobiosis and chondrocyte necrosis are detected in thespit cartilage.

In individual preparations, the places of attachment of fibrous structures to the neck of the femur and foci ofgranulation tissue are traced.

Between the cartilaginous part of the femoral head and the synovial membrane, the synovial membrane with full-blood vessels and adipose tissue are sometimes found in the joint space. Collagen fibers are loosened, homogenized. Along with this, there is an enchondral ossification with identified newly formed bone beams and multiple full-blood vessels.

The results of the studies allow us to characterize chondrocytes in focal dystrophy and inhibition of osteogenesis on the surface of the germ zone.

In a more distant period of the experiment, the dedifferentiation of the surface and transition layers of hyaline cartilage into fibrous tissue was revealed. In the deep layers of cartilage, signs of a decrease in proliferative processes and an increase in degenerative processes were noted, which led to a distortion of osteogenesis on the surface of the growth zone.

The narrowing of the area of enchondral growth due to the disappearance of the layer of proliferating chondrocytes apparently preceded its early closure.

The revealed histological changes in the componentsof the tubular bones can help predict the results of treatment of skeletal deformities, as well as their complications.

In experimental hypoparathyroidism, pronounced changes occur in the cartilaginous elements of the greater trochanter, manifested by vacuolization of chondrocytes.

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